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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/554,980	07/17/2000	RICHARD KOLESNICK	D6049	6671

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EXAMINER
HAMUD, FOZIA M

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 12/13/2002 13

Please find below and/or attached an Office communication concerning this application or proceeding.

file copy

Office Action Summary

Application No.	Applicant(s)
09/554,980	FUKS et al.
Examiner	**Art Unit**
Fozia Hamud	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Sep 30, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-4, 6, 7, and 10* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4, 6, 7, and 10* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Receipt of Applicant's arguments and amendments filed in Paper No.12 filed on 30 September 2002 is acknowledged. Claim 1 is amended.

Thus claims 1-4, 6-7 and 10 are pending and under consideration by the Examiner.

2. The following previous rejections and objections are withdrawn in light of Applicants amendments filed in Paper No.12, 09/30/02:

(I) The rejection of claims 1, 4 and 10 made under 35 U.S.C. 102(a) as being anticipated by Hamivotiz-Friedman et al (1 December 1997).

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 U.S.C. § 112

4. The rejection of claims 1, 2 and 3 made under 35 U.S.C. 112, second paragraph is maintained for reasons of record set forth in the office action mailed on 02 July 2002 in Paper NO:11 , page 2.

Applicants have amended claim 1, however, this amendment does not obviate the rejection of claims 1-3 under 35 U.S.C. 112, second paragraph. Removing the limitation "in need of such treatment", does not render claim 1 definite, because it is still unclear what is the purpose of administering b-FGF, i.e, what is the animal being treated for. Instant claim 1 is incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: instant claim 1 is drawn to a method of administering b-FGF to an animal, however, the claim does not recite what said animal is suffering from, if anything, or whether the b-FGF is being administered to a healthy animal. Furthermore, it is unclear what is the result to be

achieved from said administration. Thus, while the claim is drawn to a method of administering b-FGF to an animal, the claim fails to recite what said animal is suffering from and what result should be achieved from said administration. Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 102

5. The rejection of claims 1, 4 and 10 made under 35 U.S.C. 102(b) as being anticipated by Fuks et al (1994), is maintained for reasons set forth n the office action mailed on 27 February 2002, in paper No:9, pages 4-5 and reiterated in pages 3-5 of the office action mailed on 02 July 2002, in paper No:11.

Applicants argue that Fuks et al reference does not anticipate instant claim 1, because Fuks et al does not teach inherently or expressly that the administration of b-FGF to an animal inhibits the generation of ceramide from sphingomyelin. Applicants contend that disclosure of a particular compound in the prior art does not provide proper basis for rejection of a method claim that encompasses a previously undisclosed function of the compound even though the function may be inherent in the structure of the compound. Applicants state the it is well established that an Applicant may seek patent protection of a new use of a known compound. with respect to claims 4 and 10, Applicants argue Fuks et al do not anticipate claims 4 and 10, because Fuks et al teach the administration of basic fibroblast growth factor as a method to treat endotoxic shock or a method of treating sepsis. Thus, Applicants argue that Fuks et al make no teaching that b-FGF could be used a therapeutic treatment for radiation damage or for sepsis or endotoxic shock.

These arguments have been fully considered but are not deemed persuasive.

Fuks et al reference anticipates instant claim 1, because it does teach administration of basic fibroblast growth factor (b-FGF) to an animal. Thus, although, Fuks et al reference does not expressly teach that the administration of b-FGF leads to the inhibition of the generation of ceramide from sphingomyelin, this is an inherent property of the administration of b-FGF. The discovery of an inherent property of a prior art process can not serve as a basis of patenting that process, see Ex parte Novitski, 26 USPQ2d (Bd. Pat. App. & Inter. 1993). In the instant case, the administration of b-FGF into an animal to protect said animal from endothelial apoptosis is in the prior art of record. Applicants' assertion that the disclosure of a particular compound in the prior art does not provide proper basis for rejection of a method claim that encompasses a previously undisclosed function of the compound even though the function may be inherent in the structure of the compound, is not found persuasive, because the mere recitation of newly-discovered function or property, inherently possessed by things in prior art, does not cause claim drawn to those things to distinguish over prior art. The method of administering b-FGF into an animal, taught by Fuks et al, does inherently inhibit the generation of ceramide from sphingomyelin, unless Applicants can show otherwise, (in re Best, 195 USPQ 430, CCPA, 13 October 1977). Applicants statement that it is well established that an Applicant may seek patent protection of a new use of a known compound is correct, however, instant claim 1, does not recite a new use for the known compound. Although instant claim recites the administration of b-FGF to an animal, it does not recite what is the new use of the old b-FGF. Inhibiting the generation of ceramide from sphingomyelin is a newly discovered function for b-FGF, which is an inherent property for the structure of this protein. Therefore, since instant claim 1 does

not recite what is the new use for b-FGF, (it only recites a new function for b-FGF), the method of administering b-FGF into an animal taught by Fuks et al anticipates this claim.

With respect to claims 4 and 10, Applicants' argument that Fuks et al do not teach the administration of basic fibroblast growth factor as a method to treat endotoxic shock or a method of treating sepsis, is correct, however, instant claims 4 and 10 are drafted in such a way that they are anticipated by the Fuks et al reference. Fuks et al reference expressly teaches the administration of b-FGF into an animal, it also teaches that said administration inhibits endothelial apoptosis. Therefore, Fuks et al reference does teach all the limitations in instant claims 4 and 10, either expressly or inherently, thus, anticipating instant claims 4 and 10. Whether the reference teaches the mechanism of action claimed by Applicants or a different mechanism of action for b-FGF is irrelevant, as long as the reference teaches the claimed method, which it does, thus anticipating instant claims 4 and 10.

Claim Rejections - 35 U.S.C. § 103

6. The rejection pf claims 1, 2, 3, 4, 6 and 7 made under U.S.C. § 103 as being unpatentable over Fuks et al (1994), is maintained for reasons of record set forth in pages 6-8 of the office action mailed on 02 July 2002, in paper No:11.

Applicants argue that Fuks et al contain no suggestion that would motivate one skilled in the art to arrive at the instant invention. Applicants also argue that Fuks contains no suggestion that b-FGF could be used as a therapeutic agent for the treatment of any disease. Even if one skilled in the art could be motivated by Fuks to attempt to develop b-FGF administration as a treatment for a disease, this motivation rises to the level of being "obvious to try" and this is not the correct standard

for determining obviousness under 35 U.S.C.§ 103. Finally, Applicants argue that at minimum, arriving at the claimed methodology after a reading of the teachings of Fuks would involve an undue amount of experimentation.

These arguments have been fully considered but are not deemed persuasive. Firstly, Fuks et al teach a method of administering basic fibroblast growth factor (b-FGF) into an animal. Secondly, the researchers showed that administration of b-FGF into an animal leads to the inhibition of radiation-induced programmed cell death (endothelial apoptosis) in-vitro and in-vivo. Thus, Fuks et al have established a link between the administration of b-FGF and inhibition of endothelial apoptosis, thus providing motivation for the claimed method. Courts have found utility for therapeutic inventions despite the fact that an applicant is at a very early stage in the development of a pharmaceutical product or therapeutic regimen based on a claimed pharmacological or bioactive compound or composition. The Federal Circuit has reiterated that therapeutic utility sufficient under the patent laws is not to be confused with the requirements of the FDA with regard to safety and efficacy of drugs to marketed in the United States. FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws. Scott [v. Finney], 34 F.3d 1058, 1063, 32 USPQ2d 1115, 1120 [(Fed.Cir. 1994)]. Usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans. Therefore, Fuks et al provide more than a mere "obvious to try" motivation to arrive at the claimed method.

New rejections:

Claim rejections-35 U.S.C. § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7a. Claims 4-7 and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating endotoxic shock and sepsis by administering b-FGF, wherein said b-FGF inhibits endothelial apoptosis resulting from endotoxic shock or sepsis by inhibiting the generation of ceramide from sphingomyelin, does not reasonably provide enablement for a method of treating endotoxic shock and sepsis by administering b-FGF, wherein said b-FGF *prevents* endothelial apoptosis resulting from endotoxic shock or sepsis by inhibiting the generation of ceramide from sphingomyelin.

Claim 4 and 10 recite ".....", wherein said basic growth factor *prevents* endothelial apoptosis.....", however, the specification as filed does not disclose a single example where endothelial apoptosis is prevented. The specification is non-enabling for a method to prevent eosinophilia. Instant specification discloses that b-FGF inhibits the generation of ceramide from sphingomyelin and that b-FGF inhibits LPS induced apoptosis, *in-vivo*, (see figure 6). However, Applicants have not shown that b-FGF, prevented endothelial apoptosis. PREVENT implies taking advance measures against something possible or probable, however, Applicants have not demonstrated that giving b-FGF in advance would assure that endothelial cell death will not occur in the future. Therefore, the instant specification is non-enabling for a method of treating endotoxic shock and sepsis by administering b-FGF, wherein said b-FGF *prevents* endothelial apoptosis,

resulting from endotoxic shock or sepsis by inhibiting the generation of ceramide from sphingomyelin. By application of the factors set forth in In re Wands, page 1404, the factors which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, in the instant application, Applicants have not provided enough guidance as to how much b-FGF is to be administered to prevent endothelial apoptosis, and for how long, therefore, the quantity of experimentation to determine whether administering b-FGF would prevent endothelial apoptosis is enormous, because of the unpredictability of art and the lack of guidance by Applicants.

Thus, Applicants are non-enabling for a method of treating endotoxic shock and sepsis by administering b-FGF, wherein said b-FGF *prevents* endothelial apoptosis resulting from endotoxic shock or sepsis by inhibiting the generation of ceramide from sphingomyelin.

Claims 6-7 are rejected as under 35 U.S.C. 112, first paragraph, so far as they depend on claim 4 for the above mentioned limitation.

Claim Rejections - 35 U.S.C. § 102

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C.

122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

8. Claims 4, 6 and 10 are rejected under 35 U.S.C. 102(e) as being anticipated by Jain et al. (U. S. Patent 6,010,712).

Jain et al disclose a method of treating sepsis by administering b-FGF to an animal suffering from said condition, (see abstract, column 8, lines 26-30 and claims 1 and 2).

Instant claims 4, 6 and 10 are drawn to a method of treating endotoxic shock and sepsis in an animal (human) by administering b-FGF to said animal. Therefore, the Jain et al reference clearly anticipates instant claims 4, 6 and 10, in the absence of any evidence to the contrary.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*
>
> *Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was

commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

9. Claim 4, 7 is rejected under U.S.C. § 103 as being unpatentable over Jain et al.

The teachings of Jain et al have been set forth above, as applied to claims 4 and 10. However, Jain et al do not disclose a method of administering b-FGF into an animal using the specific doses and times recited in claim 7.

Jain et al teach a method of administering b-FGF into an animal to treat sepsis.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention, to design a method of administering b-FGF and to optimize both the dosage and duration of said administration to get the benefits of this protein, because Jain et al taught that b-FGF treats sepsis. One of ordinary skill in the art would have been motivated to optimize the duration and the dosage of b-FGF administration, because, Jain et al teach that optimal dosage for a given patient depends upon weight, age and gender and can be determined by one of ordinary et al in the art, (see 6,010,712, column 8, lines 48-55).

Conclusion

10. No claim is allowed.

Applicants have discovered a new property of b-FGF; that b-FGF inhibits the generation of ceramide from sphingomyelin. Applicants demonstrate that b-FGF inhibits accumulation of tissue ceramide induced by LPS (see table II), and that b-FGF abrogates LPS induced apoptosis, *in-vivo*,

(see figure 6). However, the claimed method is not patentable over the prior art of record, (the mere recitation of newly-discovered function or property, inherently possessed by things in prior art, does not cause claim drawn to those things to distinguish over prior art), unless Applicants identify a patient population that can benefit from the new property of b-FGF, said patient population being different from the prior art patient population that takes b-FGF.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia Hamud whose telephone number is (703) 308-8891. The examiner can normally be reached on Mondays-Thursdays from 8:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary kunz can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit 1647
11 December 2002

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